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NORMA E HENDERSON
HENDERSON PATENT LAW
13 JEFFERSON DR
LONDONDERRY, NH 03053

| EXAMINER | |
|---|---|
| LUNDGREN, JEFFREY S | |
| **ART UNIT** | **PAPER NUMBER** |
| 1639 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/622,126 | JACOBSON ET AL. | |
| | Examiner | Art Unit | |
| | Jeff Lundgren | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *1-37 and 43-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *see office action*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Claims*

Claims 1-50 are pending in the application, claims 38-42 are being examined on the merits and claims 1-37 and 43-50 are withdrawn.

### *Information Disclosure Statement*

The information disclosure statements (IDS) submitted on October 11, 2006, and October 12, 2006, have been considered by the Examiner. The submissions are in compliance with the provisions of 37 CFR § 1.97. Enclosed with this Office Action is a return-copy of the Form PTO-1449 with the Examiner's initials and signature indicating those references that have been considered. The references cited on the IDS submitted on October 12, 2006, are duplicates and are so indicated.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 38-42 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Accordingly, Applicants do not have written description support for the claimed subject matter.

Applicants generally argue that where their application is lacking in support, that sufficient support is provided in the art. Applicants reference Gartner, Jacobsen, Hamad-Schiffereli, Hess, Manashi and Reif, and allege that one of ordinary skill in the art could find the requisite guidance in these references. Regarding Gartner, it is argued that Gartner teaches a range of reaction types. Applicants argue that in Jacobsen, chemically synthesized, cell-permeable, non-natural precursors were transformed into molecules resembling natural products

by genetically engineered polypetide synthases. Applicants suggest that remote electronic control over the hybridization behavior of DNA molecules is achieved by inductive coupling of a radio-frequency magnetic field to a metal nanocrystal covalently linked to DNA (Hamad-Schifferli at page 152, col. 2), and that the work of Hamad-Schifferli demonstrates that individual nanocrystals can be removed while leaving surrounding molecules unaffected, which reaction is fully reversible. In Hess, Applicants argue that microtubules, covalently loadable with cargo, were moved on engineered kinesin tracks, and surmises Hess as noting that the disclosed structures were useful as components for the construction of nanoscale assembly lines.

Applicants arguments have been fully considered, but are not found persuasive for the following reasons. Regarding Gartner, it is inapposite that Gartner teaches a range of reaction types. Gartner does not relate to the "translatable molecular shuttle"; similar is the argument regarding Jacobsen and Hamad-Schifferli. Regarding Hess, the translocation of the nanostructures is also outside the scope of Applicants claim, and does little to shine light on the claimed device having translatable molecular shuttle. Furthermore, Hess' results do not provide the requisite guidance where Applicants' disclosure is lacking, such as the translocation of microtubes with bond breaking and forming (nor do Manashi's teachings or footnotes).

As stated in the previous Office Action, the written description requirement is distinct from the enablement requirement; this was first pointed out by the court in *In re Ruschig*, 379 F.2d 990, 154 USPQ 118 (CCPA 1967), and clarified in *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991). The issue of whether the claimed subject matter is adequately supported/described by the specification, is a question of *fact*. *Id.* at 1563, 19 USPQ2d at 1116.

When considering whether the claimed subject matter complies with the written description requirement, Applicants' disclosure should be read in light of the knowledge possessed by those skilled in the art.

> "[T]he disclosure in question must be read in light of the knowledge possessed by those skilled in the art, and that knowledge can be established by affidavits of fact composed by an expert, and by referencing to patents and publications available to the public..."

*In re Lange*, 644 F.2d 856, 863, 209 USPQ 288, 294. *See also, In re Alton*, 76 F.3d 1168, 37 USPQ2d 1578 (Fed. Cir. 1996).

Applicants enjoy the presumption that their patent application is valid and all statements contained therein are accurate; it is the PTO's burden to demonstrate why any of Applicants claims should be rejected or why any of Applicant's statements should be doubted.

> "it is incumbent upon the Patent Office, whenever a rejection... is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure."

*In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370. If successful in presenting such evidence and argument, the burden then shifts to the Applicant to provide evidence that would convince one to the contrary.

***The Invention in General***

A significant component of Applicants' invention is directed to a molecular assembly line capable of controlling the binding of certain molecular units, controlling certain chemical reactions at a given molecular assembly site, applying an input signal and causing a nanoscale movement or shift in the molecule, and applying another chemical reaction for adding a subsequent molecular unit onto the molecule.

Accordingly, such an invention requires a device that is capable of controllably moving molecules in a desired manner with nanoscale and/or angstrom-level precision. The claimed invention also requires the ability to apply energy inputs on the order of magnitude of a chemical bond at a given molecular region *via* the use of Applicants' assemble line, and then to chemically react a subsequent molecular unit onto the substrate at the desired location.

***The Supporting Disclosure***

Applicants describe in their specification how molecular "shuttles" have been studied in recent years, but note that a molecular assembly line has yet to be constructed (pages 1 and 2).

Applicants further list a number of embodiments of the claimed invention and certain components utilized (pages 3-4).

A generalized description of the invention components is listed, and certain embodiments, and certain operational aspects are noted (pages 7-11). Applicants summarize their figures and list certain elements as they pertain to the claimed invention (11-28).

For examples, Applicants have an example of selective dehybridization (*i.e.*, a shuttle, not an assembly line; pages 28-32), and an illustration of certain photochemical cleavage reactions (pages 32-35). There is ***no working example*** of the claimed invention, *i.e.*, the molecular assembly line.

***The State of the Art***

As it is with many biotechnology inventions, the relevant art is multidisciplinary. Applicant's claimed invention relates to a number of core technologies and scientific concepts including nanopatterning and controllably moving molecules on the nanoscale *via* controllable inputs/forces. Accordingly, those of skill in the art have a firm understanding of the inter-relationship between each of the disciplines and the functional and physical limitations of the claimed invention, and is pertinent in determining the level of skill in the art. Taken as a whole, the relevant art suggests that Applicant was neither in possession nor had written description support for the claimed invention at the time the application was filed.

The cited references raise a number of factual considerations that reasonably challenge Applicant's disclosure, and would lead one of ordinary skill in the art to doubt that Applicant had adequately described the claimed molecular assembly line.

In general, one major obstacle in constructing Applicants' claimed assembly line is the required atomic resolution for surface immobilized components, such as DNA. For example, each of Ge and Demers illustrate that current methods of construction do not reach the angstrom level of precision required by Applicants' assembly line (Ge *et al.*, *Biosensors and Bioelectronics 18*:53-58 (**2000**), and Demers *et al.*, *Science 296*:1836-1838 (**2002**)). See each of the figures in Ge and Demers, and note that the molecular resolution is not even on the nanometer or angstrom level scale.

Another significant obstacle concerns the controlled movement required by Applicants' device. For example, Applicants suggest that they can control dissociation and association reactions of neighboring molecular sites, and thereby shift a substrate molecule down the chain by a single molecular unit. Applicants allege that a component of this may involve the use of, for example, an optical probe (page 16, paragraph 0059). However, numerous dye molecules are routinely excited and do not cause the effects identified by Applicants, for example, as in Hamad-Schifferli (see Figure 3 and description thereof, Hamad-Schifferli *et al.*, *Nature 415*:152-155 (**2002**)). Further, Hamad-Schifferli shows that molecules can be removed, but does not show the "shifting" as claimed by Applicants. This would require the ability to apply just enough force to cause dissociation at one given site, and at a neighboring site apply a force to cause association, all occurring on the time scale of diffusion over molecular distance (sub-nanosecond for these distances). Applicants' disclosure hardly takes into consideration the highly intricate considerations of these factors.

Generally, there is a reasonable level of doubt that would suggest that Applicant's has not met the written description requirement. Applicants do not provide a description that reasonably overcomes the factual understanding that is indicative of the state of the art. The greater part of the claimed invention relies on oversimplified illustrations that significantly omit practical real world physicochemical considerations as cited above. One of skill in the art would find these factors essential in considering the practical application for creating and using such an assembly line.

### *Claim Rejections - 35 USC § 102*

The rejection of the claims as being anticipated by Guatelli and by Hamad-Schifferli is withdrawn in view of Applicants amendment to the claims.

### *Conclusions*

No claim is allowable.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

If Applicants should amendment the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsis verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, James Schultz, can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSL

JAMES SCHULTZ, PH.D.
PRIMARY EXAMINER